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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/670,119	06/25/96	NG G	SIM-001(7434

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EXAMINER	
HAYES,R	
ART UNIT	**PAPER NUMBER**
1645	17

DATE MAILED: 04/28/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/670,119	Applicant(s) Ng et al
	Examiner Robert C. Hayes	Group Art Unit 1645

☒ Responsive to communication(s) filed on 1/25/99 .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *18, 20-37, and 60-65* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *18, 20-37, and 60-65* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 14

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 12/07/98 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/670119 is acceptable and a CPA has been established. An action on the CPA follows.

2. The objection of claims 62 & 64-65 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, is withdrawn due to the amendment of the claims.

3. The rejection of claims 18, 20-22, 36 & 60-61 under 35 U.S.C. 102(b) as being anticipated by Lofts et al., is withdrawn solely because of the apparent closed language of "consisting essentially of at least four consecutive amino acid residues". It should be noted that this rejection may be re-instated should Applicants amend the claims to overcome the rejection under 35 U.S.C. 112, second paragraph.

4. The rejection of claims 18, 20-24, 29, 36-37 & 60-61 under 35 U.S.C. 102(e) as being anticipated by Murphy et al., is withdrawn solely because of the apparent closed language of "consisting essentially of at least four consecutive amino acid residues". It should be noted that

this rejection may be re-instated should Applicants amend the claims to overcome the rejection under 35 U.S.C. 112, second paragraph.

5. Applicant's arguments filed 01/25/99 have been fully considered but they are not deemed to be persuasive.

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. Claims 18, 20-37 & 60-65 are again rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons made of record, and as follows.

Applicants argue the following six points of the previous Office action:

1) peptides "associated with specific receptor overactivity" have not been claimed; nor have they been adequately described.

Applicants argue on pages 6-7 of the response that "the claims, as amended, refer to the treatment of a disorder ... to *specifically inhibit* the activity of the integral membrane protein". In contrast, the claims recite no "specific" receptor to be inhibited, nor do they recite structurally defined components to practice the instant invention, in which each G-protein receptor

dysfunction characterizes its own unique disease state, as previously made of record. For example, claim 27 is dependent back to claim 18, which recites no specific "integral membrane protein", nor any structurally characterized peptide, in contrast to Applicants' assertions on page 7 of the response. Therefore, the claims fail to specify how the skilled artisan knows when they have successfully practiced the instant invention, without requiring undue experimentation to discover how to make and use Applicants' invention, as previously made of record.

2) although adrenergic receptor antagonists may be accepted as therapeutic agents for treatment of hypertension (i.e., as described on page 23, lines 29-30), the specification provides apparently contradictory guidance on how "heart rate [can be decreased] using a β1-adrenergic-specific peptide" (pg. 41), because vehicle alone gave a comparable change in blood pressure when compared to administrating the β1-adrenergic-specific peptide (pg. 42). Thus, treatment of hypertension does not appear to work using these transmembrane peptide molecules (i.e., as it relates to claims 30-31).

Applicants argue on pages 7-8 of the response that the amendment to the specification indicates that "the α1A- and β1-adrenergic receptor antagonist peptides... are *specific* peptides which *specifically inhibit* those receptors", as it apparently relates to claims 12-15. In contrast to Applicants' assertions, claims 12-15 are cancelled. Moreover, none of claims 18, 21, 22, 23, 29-30 and 33 distinguish between specific α1A- and β1-adrenergic receptor antagonist peptides *and* treating "cardiac arrhythmia", versus "hypertension" (i.e., as it relates to amended

claims 32 and 35). Thus, the issue remains that the specification is clearly deficient in providing sufficient guidance for knowing how to effect measurable phenotype as it relates to generic adrenergic receptors, as currently claimed, without requiring undue experimentation to determine such, for the reasons made of record.

3). although theophylines may work on adenosine receptors as anti-asthmatics, and caffeine may have antidepressant effects though antagonizing adenosine receptors, the claims do not recite using any specific peptide to specifically "decrease asthma" or "decrease depression" or "decrease arrhythmia" through "antagonizing specific adenosine receptors" (i.e., A1, A2a, A2b or A3), which are further unknown, or not adequately conceptualized within the instant specification, as it relates to specific disease states.

Applicants argue on pages 8-9 of the response that "the claims relate to a method of treating 'a disorder for which administration of an *antagonist* of an integral membrane protein... is *indicated.*" However, as previously made of record, the claims do not recite what structurally constitutes "an antagonist...", nor what disorder or symptom is to be treated, each with their own unique etiology, nor when the skilled artisan is knows when, where or what "is indicated", because no such recitation is claimed so that the skilled artisan knows when they are in possession of the necessary components to practice the instant invention; thereby, requiring undue experimentation to determine such, for the reasons made of record. It is again noted that most neurodegenerative disease states, such as Huntington's disease, are characterized by dead and

dying neurons, which cannot reasonably be "treated", as previously made of record. Accordingly, there is no nexus for any expectation that merely administrating transmembrane-specific peptides for affecting one symptom of one disorder can be extrapolated to "treating" the full scope of symptoms encompassed by the current claim language.

4) EGF receptors are not representative of all "neoplastic growth in cancer" because all neoplasms are not caused by dysfunction of the EGF receptor, or due necessarily to dysfunction of any different receptor; each with their own unique structure and mode of action.

Applicants argue on page 9 of the response that "the claims encompass only treatment of such disorders in which administration of an *antagonist* of an integral protein *is indicated*", as it apparently relates to the EGF receptor, and that "[t]he claims are not directed to treating all neoplastic growths or, indeed, any conditions in which administration of an antagonist of an integral membrane protein is not indicated". In contrast to Applicants' assertions, no where in the claims is there any recitation to indicate when such administration "is not indicated"; thereby, encompassing all neoplastic growths, as previously made of record. As also made of record, the claims do not recite using any specific peptide to specifically "inhibit growth" of any tumor, whose etiology is otherwise unknown, and not disclosed. Thus, one skilled in the art could not reasonably practice the invention as currently claimed, without undue experimentation to discover what defects which cause cancer may then be amenable to treatment using transmembrane peptides, as previously made of record.

5) As previously made of record, GABA receptors are not representative of any different population of neurons within the brain. Nor would these intrinsically inhibitory neurons be affected by antagonists to inhibit "overactivity", based solely on drugs such as benzodiazepines, because benzodiazepines bind to "agonist sites" (see pg. 27 of the specification), versus "antagonist sites", and increase chloride influx into GABA-nergic cells; thereby inhibiting action potentials. Thus, the specification still provides contradictory evidence on how to determine how and when to successfully practice the invention, without requiring undue experimentation to discover how to make and use Applicants' invention. Accordingly, the claims do not recite using any specific peptide to specifically "inhibit GABA receptors" that effects any measurable phenotype, and as such merely represent an invitation to experiment.

6) As previously made of record, the claims still fail to recite using any specific peptide to specifically "inhibit dopamine and/or monoamine transporters" that effect any measurable cell type, disease state, or measurable phenotype; and as such merely constitutes an invitation to discover how to make and use Applicants' invention, thereby, not being enabled, for the reasons made of record.

In summary, the claims remain not commensurate in scope with the limited guidance provided by the specification on how to successfully practice the instant invention without undue experimentation to discover how to make and use Applicants' invention; especially in this very unpredictable art of treating disease states that have their own unique, and unknown, etiologies, for the reasons extensively made of record.

8. Claims 18, 20-37 & 60-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear when "administration of an antagonist ... is *indicated*" when no such step is recited in the claims, or what "disorder" is to be "treated" when none is recited in the claims.

The claims 18 and 36 (as well as all dependent claims) are indefinite because of the new recitation " consisting essentially of... amino acid residues", in which a peptide is defined by its amino acid sequence and in which different sequences change the peptide being claimed, by definition. Thus, amino acid residues cannot "consist essentially of", by definition. Further, it appears contradictory for a peptide to "consist essentially of *at least* four consecutive amino acid residues", when "consisting essentially of" encompasses deleting amino acid residues; thereby, being less than four amino acid residues.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and on alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
April 20, 1999

Patricia A. Duffy
PATRICIA A. DUFFY
PRIMARY EXAMINER